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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/639,207	KAZEMI-ESFARJANI ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- Th MAILING DATE of this communication appears on th cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,29-35,37-40 and 42-79* is/are pending in the application.

4a) Of the above claim(s) *47-49 and 51-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,29-34,37-40,42,43 and 50* is/are rejected.

7)☒ Claim(s) *35 and 44-46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This Non-Final Office Action is a response to the "Response" filed 11 June 2003 (Paper No. 14) in reply to the Final Office Action mailed 20 March 2003 (Paper No. 12). Claims 1-3, 7, 9-26, 29-46 and 50 were considered in Paper No. 12. Claims 1-25, 36 and 41 were canceled and claims 26, 37 and 39 were amended in Paper No. 14. Claims 26, 29-35, 37-40 and 42-79 are pending and claims 26, 29-35, 37-40, 42-46 and 50 are under consideration.

Response to Amendment

Rejection of claims 1-25, 36 and 41 is rendered moot by cancellation of the claims.

Claim Rejections - 35 USC § 112

Rejection of claims 26, 29-35, 36-40 and 42-46 under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claimed subject matter is withdrawn in view of the amendments to the claims.

Claim Rejections - 35 USC § 102

Rejection of claims 37 and 39 under 35 U.S.C. 102(b) as being anticipated by Warrick et al. (1998) *Cell* 93:939-949 as evidenced by Paulson (1997) *Neuron* 19:333-344 is withdrawn in view of the amendments to the claims.

New grounds for rejection are set forth below.

New Grounds

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42 and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Claim 42 is directed to a *D. melanogaster* comprising a marker sequence inserted into its genomic DNA, wherein the marker is located adjacent to a gene or inserted in a gene whose expression or activity increases or decreases polyglutamine toxicity in the animal. Thus the claims encompass a genus of *D. melanogaster* comprising marker located adjacent to any and all genes or inserted in any and all genes whose expression or activity increases or decreases polyglutamine toxicity in the animal, wherein the *D. melanogaster* further comprises the limitations of claim 26. Claim 43 limits the gene of claim 42 to a gene comprising a J domain.

The Guidelines for Written Description state "The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (Federal Register, Vol. 66, No. 4, Column 3, page 71434). As the *D. melanogaster* of the claims are defined by comprising a marker sequence inserted only adjacent to or within a gene whose expression or activity increases or decreases polyglutamine toxicity in the animal, said gene whose expression or activity increases or decreases polyglutamine toxicity in the animal is a critical element of the claim. Thus, adequate written description of the claimed subject matter requires description of a gene whose expression or activity increases or decreases polyglutamine toxicity in the animal such that the skilled artisan could distinguish the subject matter encompassed by the claims from subject matter not encompassed by the claims (i.e., a *D. melanogaster* comprising a marker sequence inserted into its genomic DNA, wherein the marker is located adjacent to a gene or inserted in a gene that does not increase or decrease polyglutamine toxicity).

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics (see MPEP 2163 (ii)). In the instant case, Applicant has described three genes having the property of increases or decreases polyglutamine toxicity in the animal. However, the Guidlines state, "[s]atisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the genus in view of the species disclosed (*Id.* at 1106, column 3). The necessary common

attributes or features of the genus of genes whose expression or activity increases or decreases polyglutamine toxicity in the animal is not apparent from the species set forth, and Applicant fails to provide any guidance with regard to what the necessary common attributes might be. Beyond the three disclosed species, genes whose expression or activity increases or decreases polyglutamine toxicity are identified solely by function with no disclosure of a correlation between structure and function.

Although Applicant discloses a method of identifying said *D. melanogaster* comprising a marker sequence inserted only adjacent to or within a gene whose expression or activity increases or decreases polyglutamine toxicity, adequate written description of a transgenic animal requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. What is required is a description of the animal itself. It is not sufficient to define an animal solely by the position of a marker gene in its genome without describing in specific terms where the marker gene will be positioned. That is, disclosure of no more than that the marker will be positioned in a gene having a given function without identifying the gene, as in the instant case, is simply a wish to know the identity of any animal with that property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all animals that have a marker located in a gene whose expression or activity increases or decreases polyglutamine toxicity without defining the gene is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed

invention commensurate to its scope because it does not provide adequate written description for the broad class of *D. melanogaster* comprising a marker sequence inserted into its genomic DNA, wherein the marker is located adjacent to a gene or inserted in a gene whose expression or activity increases or decreases polyglutamine toxicity in the animal. Therefore, only the described species wherein the gene is HDJ1, TPR2 and MLF meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26, 29-34, 37-40 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Warrick et al. (1998) *Cell* 93:939-949 (previously made of record) as evidenced by Paulson (1997) *Neuron* 19:333-344 (previously made of record). Although the claims were previously indicated to be free of the art, upon further consideration it is apparent that the limitations of the claims would have been obvious to one of ordinary skill in the art at the time the instant application was filed.

Claims 26, 29-34, 37-40 and 50 are drawn to a transgenic *Drosophila* comprising a transgene containing a plurality of CAG's and at least one CAA sequence encoding a polyglutamine repeat sequence, wherein the repeat comprises at least 100 contiguous glutamine residues. Claims 29-32 limit the number of CAG's to CAA's to various ratios ranging from of 1:1 to 50:1; claim 33 limits the control element for expression of the polyglutamine sequence to a constitutive, regulatable or tissue specific control element; claim 34 limits the tissue specific control element of claim 33 to a control element that confers neural, retinal, muscle or mesoderm cell expression. Claim 37 limits the polyglutamine sequence to between 100 and 150 amino acids in length; claim 38 limits the polyglutamine sequence to between about 100 and 200 amino acids

in length; claim 39 limits the polyglutamine sequence to between about 100 and 250 amino acids in length; and claim 40 limits the polyglutamine sequence to a sequence further comprising a tag. Claim 50 is drawn to a method of producing a transgenic *Drosophila* characterized by polyglutamine toxicity comprising: (a) transforming a *Drosophila* embryo or fertilized egg with a transgene comprising a plurality of CAA and CAG sequences encoding a polyglutamine sequence comprising at least 100 contiguous glutamine residues; and (b) selecting a *Drosophila* that exhibits polyglutamine toxicity in one or more tissues.

Warrick teaches a transgenic *Drosophila melanogaster* comprising a transgene containing a plurality of CAG's and at least one CAA wherein the CAG's and CAA's are present in a ratio of about 40:1 (two CAA resides in a total of 78 codons) and fused to a hemagglutinin epitope tag (see especially the description of the MJD construct on page 948 beginning the final sentence of column 1 and continuing through the first paragraph of column 2; also see the attached sequence file showing the codons comprised within the polyglutamine portion of the MJD1 coding sequence, this sequence was expanded to 78 glutamines by insertion of CAG repeats (see Paulson page 342, first paragraph of column 2)). Warrick also teaches targeted expression of an expanded polyglutamine sequence wherein the promoter comprises an inducible promoter comprising a GAL4 responsive sequence, wherein tissue specific expression (i.e. neural, mesoderm, muscle and eye specific expression) is conferred through tissue specific expression of GAL4 (see especially the second column of Table 1 on page 940). Warrick also teaches a method of producing a transgenic *Drosophila* characterized by polyglutamine toxicity comprising generating transformant lines by "standard procedures" (final sentence of the first paragraph in the second column of page 948), which one of ordinary skill in the art would

understand to comprise transforming a *Drosophila* embryo or fertilized egg with the transgene, and selecting a *Drosophila* that exhibits polyglutamine toxicity in one or more tissues (see especially Table 1 and the caption thereto).

Warrick does not teach a polyglutamine repeat comprising at least 100 contiguous glutamine residues or ratios of CAG's to CAA's between 1:1 and 2:1, 2:1 and 5:1, and 5:1 and 10:1. However, the MPEP states, "a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. Titanium Metals Corp. of America v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)" (§§2144.05). In the instant case, Warrick teaches a transgenic *Drosophila* comprising a polyglutamine sequence of 78 residues, which is demonstrated to produce polyglutamine toxicity in the transgenic fly. The limitation of at least 100 contiguous glutamine residues is very close to the 78 glutamine residues reduced to practice by Warrick. In view of this, one of ordinary skill in the art would clearly expect the transgenic *D. melanogaster* of Warrick to have the same properties as the transgenic *D. melanogaster* of the instant claimed invention (i.e., polyglutamine toxicity). Thus, the claimed invention would have been obvious to one of ordinary skill in the art at the time the application was filed. For this same reason, the instant claimed method of making a transgenic *Drosophila melanogaster* would have been obvious to one of ordinary skill in the art at the time the application was filed in view of the method described by Warrick. With regard to the ratios of CAG's to CAA's, the skilled artisan would expect that the properties of the transgenic *D. melanogaster* comprising a polyglutamine repeat of sufficient length to induce polyglutamine toxicity would be the same regardless of the codon ratio comprised within the polynucleotide encoding the polyglutamine repeat. Thus,

absent evidence to the contrary, the limitations of 26, 29-34, 37-40 and 50 would have been obvious to one of ordinary skill in the art at the time the instant application was filed.

Claims 26 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Warrick et al. (*supra*) as evidenced by Paulson, as applied above to claim 26, and in view of Rørth (1996) *Proc. Natl. Acad. Sci. U.S.A.* 93:12418-12422 (previously made of record). Although the claims were previously indicated to be free of the art, upon further consideration it is apparent that the limitations of the claims would have been obvious to one of ordinary skill in the art at the time the instant application was filed.

The limitations of claim 26 are set forth herein above. Claim 42 is drawn to the a transgenic *Drosophila* of claim 26, further comprising a marker sequence inserted into its genomic DNA wherein the marker is located adjacent to a gene or inserted into a gene whose expression or activity increases or decreases polyglutamine toxicity in the animal, and wherein the marker sequence comprises an inducible upstream activating sequence, a minimal promoter sequence and 5' and 3' transposon elements containing terminal inverted repeats.

Warrick teaches a *Drosophila* expressing a polyglutamine sequence, wherein the sequence produces polyglutamine toxicity (see especially Table 1 and the caption thereto) and that the *Drosophila* expressing a polyglutamine sequence can be used with, "*Drosophila* genetics to identify genes that can delay or prevent deleterious consequences of the polyglutamine-repeat proteins on neuronal integrity". Warrick does not teach a *Drosophila* further comprising a marker sequence inserted into its germline, wherein the marker sequence comprises 1) an inducible upstream activating sequence, 2) a minimal promoter sequence and 3) 5' and 3'

transposable elements or a transgenic *D. melanogaster* comprising a polyglutamine repeat of at least 100 contiguous glutamine residues. However, for reasons set forth above, the *D. melanogaster* comprising a polyglutamine repeat of 100 or more contiguous glutamine residues would have been obvious to one of ordinary skill in the art based on the teachings of Warrick alone.

Rørth teaches a *Drosophila* having a marker sequence inserted into its germline, wherein the marker sequence comprises 1) an inducible upstream activating sequence, 2) a minimal promoter sequence and 3) 5' and 3' transposable elements and identifying genes operationally-associated with the marker sequence (see especially page 12421, column 2, first to third full paragraph). Rørth also teaches that, "[c]ontrolled overexpression can also identify important genetic interactions; if increased expression of one gene enhances or suppresses the phenotype of a mutation in another gene, their products are likely to be involved in the same process" (page 12418, column 1, final paragraph of column 1).

In combination, Warrick and Rørth teach all of the limitations of the broadest embodiment of the claimed invention. Further, they each teach that their methods can be combined with other methods for the purpose of identifying genes that interact with mutant genes (i.e. Warrick teaches using *Drosophila* genetics to identify genes that delay or prevent polyglutamine-repeat toxicity and Rørth teaches using controlled overexpression to identify gene interactions). Thus, Warrick and Rørth provide direction and motivation to breed their respective *Drosophila* to produce the transgenic *Drosophila* of claim 42. Therefore, the claimed progeny would have been obvious to one of ordinary skill in the art at the time the invention was made.

As, the materials and teaching to combine the materials to produce the claimed invention were available to the skilled artisan prior to the effective filing date of the application, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Warrick and Rørth according to the teachings of the instant application. Motivation to combine these teachings comes from Warrick, who teaches that the fly model of polyglutamine toxicity can be used to identify additional genes that can mitigate neurodegeneration in humans (page 940, final sentence of the first full paragraph), and from Rørth who teaches that the methodology described provides "a novel genetic approach to link genes and function in higher eukaryotes: identifying genes that, when over- or misexpressed...modulate an existing mutant phenotype" (page 12422, first full paragraph, emphasis added). A reasonable expectation of success is also provided by Warrick, who teaches, "[o]ur studies with *P35* indeed demonstrate that this system can effectively be used to define genes or factors that can mitigate degeneration" (page 948, second full paragraph) and Rørth who teaches, "target lines are easy to generate and...induced, mutated genes are easily identified" (page 12422, first full paragraph).

Because Warrick and Rørth teach all of the limitations of the claims and, as described above, provide both direction and motivation to combine their independent teachings to produce the claimed *D. melanogaster*, the claims would have been obvious to one of ordinary skill in the art at the time the invention was made.

In response to the rejection of claims as unpatentable over the teachings of Warrick *et al.* in view of Rørth in previous Office Actions, Applicant argues in Paper No. 14 that the teachings

of Warrick *et al.* and Rørth do not render the teachings of the instant application obvious because the skilled artisan would not be motivated to combine the teachings.

In response to arguments by the Examiner set forth in Paper No. 12, wherein the Examiner asserts that Warrick suggests combining the cited references by stating, "[w]e can now use *Drosophila* genetics to identify genes that delay or prevent the deleterious consequences of the polyglutamine repeat proteins on neural integrity", Applicant points out that this statement is followed by the statement, "Our studies with P35 indeed demonstrate that this system can effectively be used to define the genes or factors that can mitigate degeneration." Applicant seems to be asserting that because Warrick demonstrates the utility of the transgenic *Drosophila* to define the genes or factors that can mitigate degeneration by introducing an exogenous gene, it would not occur to the skilled artisan in possession of the teachings of Warrick and Rørth that the *Drosophila* would also have utility to identify endogenous genes that can mitigate degeneration. It should be made clear that the level of ordinary skill in the art of *Drosophila* genetics is very high. Given this level of skill, the artisan clearly would not have interpreted the statements of Warrick regarding the use of *Drosophila* genetics to be limited only to expression of exogenous genes.

Applicant further states, "[a]t no point does Warrick or Rørth teach, suggest, mention or allude to any method that would involve altering the expression of an **endogenous** nucleic acid sequence to determine its effect on polyglutamine toxicity" (page 9). However, clearly one of ordinary skill in the art in possession of the teachings of both Warrick and Rørth would understand that *Drosophila* genetics includes altering the expression of an endogenous nucleic acid sequence to determine its effect on a mutant phenotype. As pointed out several times, Rørth

teaches that the method described therein, which is a method of altering expression of an endogenous nucleic acid sequence, can be used to identify genes that modulate an existing mutant phenotype. In view of this teaching, it would be readily apparent to one of ordinary skill in the art that the method of altering expression of an endogenous nucleic acid sequence described by Rørth could be applied to identify genes that delay or prevent the deleterious consequences of the polyglutamine repeat proteins on neural integrity, which is the explicitly stated use for the transgenic *Drosophila* of Warrick. Thus, the teachings of Warrick and Rørth, viewed as a whole, clearly would suggest to one of ordinary skill that the teachings set forth therein could be combined for the purpose altering the expression of an endogenous nucleic acid sequence to determine its effect on polyglutamine toxicity.

Applicant states, "[the general statement of Warrick *et al.*] predicting that *Drosophila* genetics can be used to identify genes that modulate the effects of polyglutamine expression cannot make obvious all succeeding methods for accomplishing this goal using transgenic *Drosophila*" (page 9). This argument is not persuasive because it is the combined teachings of Warrick and Rørth, not the statement of Warrick alone, which is the basis for the obviousness rejection. Warrick teaches using *Drosophila* genetics to identify genes that delay or prevent polyglutamine-repeat toxicity and Rørth teaches using controlled overexpression by a process that would clearly fall within the definition of *Drosophila* genetics to identify gene interactions and explicitly states that the method can be used to identify genes that modulate an existing mutant phenotype.

Applicant argues that the rejection is based on a conclusion that the claimed method is obvious because those skilled in the art would allegedly know that the teachings of Warrick

encompass those of Rørth. Rørth teaches a method of producing controlled overexpression of an endogenous gene comprising inserting a marker sequence in to the germline of a transgenic *Drosophila*, wherein the marker sequence comprises 1) an inducible upstream activating sequence, 2) a minimal promoter sequence and 3) 5' and 3' transposable elements and identifying genes operationally-associated with the marker sequence. Rørth further teaches, "[c]ontrolled overexpression can also identify important genetic interactions; if increased expression of one gene enhances or suppresses the phenotype of a mutation in another gene, their products are likely to be involved in the same process" (page 12418, column 1, final paragraph of column 1). The skilled artisan would clearly view the teachings of Rørth as *Drosophila* genetics. Therefore, although Warrick does not explicitly state that teachings of Rørth should be applied to alter the expression of an endogenous nucleic acid sequence to determine its effect on polyglutamine toxicity, in which case the claims would have been anticipated by Warrick, the statement from Warrick clearly suggests using methods such as the method described by Rørth to identify genes that alter polyglutamine toxicity. This suggestion, coupled with the statements from Rørth indicating that the method described therein can be used to identify genes that modulate an existing mutant phenotype, clearly suggest combining the teachings according to the teachings of the instant Application.

Finally, Applicant argues that the claims would not be obvious to the ordinary skilled artisan because Warrick fails to teach or suggest a method of identifying native *Drosophila* genes not previously associated with modulation of polyglutamine toxicity as capable of such activity. Further, Applicant argues that the claims would not be obvious to the ordinary skilled artisan because Rørth fails to teach or suggest the desirability of using the method to identify sequences

that can modify polyglutamine toxicity. These arguments are not found persuasive because, as described above, Warrick *et al.* clearly teaches that the transgenic *Drosophila* described therein has utility to identify genes that delay or prevent the deleterious consequences of the polyglutamine repeat proteins on neural integrity using the methods of *Drosophila* genetics. Given the high level of skill in the art, the skilled artisan would plainly understand that this teaching implies identifying native *Drosophila* genes not previously associated with modulation of polyglutamine toxicity as capable of such activity. The alternative is that the skilled artisan would somehow interpret *Drosophila* genetics to be limited only to manipulation of non-native *Drosophila* genes such that identification of only non-native *Drosophila* genes that delay or prevent the deleterious consequences of the polyglutamine repeat proteins is contemplated by Warrick *et al.* Such an interpretation defies common sense. Next, although Rørth does not explicitly teach using the method to identify sequences that can modify polyglutamine toxicity, in which case the claims would be anticipated by Rørth, Rørth explicitly teaches using the method to identify sequences that can modulate an existing mutant phenotype. Therefore, the teachings of the prior art, viewed as a whole, would render the claimed subject matter obvious to one of ordinary skill in the art at the time the application is filed.

Applicant submits that the teaching to combine what was available in the art comes not from Warrick and Rørth but from the claims being rejected. Applicant thus suggests that the rejection is based on a hindsight reconstruction of the claims. However, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge

gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The reasoning set forth for the rejection of record relies solely upon the teachings of the cited art and therefore is proper. Therefore, the subject matter of claims 26 and 42 would have been obvious to one of ordinary skill in the art at the time the instant application was filed.

Allowable Subject Matter

Claims 35 and 44-46 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Anne-marie Falk

ANNE-MARIE FALK, PH.D
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

dms
June 18, 2003